UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic
Addr ss: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/776,190	01/24/97	JOSEL H	P564-7002

HM12/0815

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EXAMINER	
RICIGLIANO,J	
ART UNIT	**PAPER NUMBER**
1627	23

DATE MAILED: 08/15/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/776,190	Josel et al.
Examiner	**Group Art Unit**
Joseph W. Ricigliano	1627

☒ Responsive to communication(s) filed on *May 30, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *72-99* is/are pending in the applicat

Of the above, claim(s) *78, 79, 82, and 89-99* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *72-77, 80, 81, and 83-88* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. This action is responsive to the election of 5/30/2000.

2. Applicants' election with traverse of Group I with the species of an amino acid based carrier, a hormone hapten and metal chelate markers in Paper No. 22 is acknowledged. The traversal is on the ground(s) that the inventions should not be restricted under 371 practice because the have unity of invention. This is not found persuasive because the instant application is filed under 1.53(d) and is no longer subject to unity of invention but rather to restriction practice under 35 USC 121. Moreover, even if unity of invention were the standard by which the claims were to be restricted the art cited in previous actions clearly shows that there is no special technical feature which joins inventions.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 72 -99 are pending in the instant application.

4. Claims 90-99 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicants timely traversed the restriction (election) requirement in Paper No. 22.

5. Claim 78, 79, 82 and 89 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicants timely traversed the restriction (election) requirement in Paper No. 22.

6. Claims 72-77, 80-81, 83-88 are pending in the instant application and being examined to the extent of the elected species.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 72-77, 80-81, 83-88 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

9. Claims 72-77, 80-81, 83-88 recite that the monomeric units of the carrier are selected from at least one of nucleotides, nucleotide analogs and amino acids. This would result in carriers having a mixture different monomers in the same carrier. The disclosure as originally filed does not appear to support carriers having such a mixture. Applicants can overcome this rejection by indicating where support can be found in the disclosure as originally filed. Applicants are respectfully reminded that as set forth in MPEP 714.02, applicant(s) should specifically point out where support may be found in the disclosure as originally filed for any amendments, also see 37 CFR 1.111© and MPEP § 2163.06.

10. Claims 72, 86 and 87 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey

to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Applicants' claims recite conjugates where in the haptens are hormone metabolites However, the specification discloses only a few subgeneric examples of hormone metabolites on page 8. The disclosure also does not set forth any way of obtaining or identifying all hormone metabolites so that the full scope of the genus can be ascertained. These are neither representative of the claimed genus nor does it represent a substantial portion of the claimed genus. As the claimed conjugates having hormone metabolites as a hapten are recited only by a precursor (the hormone) and not the product of metabolism itself, and no features of the metabolites themselves are set forth in the claims, one of ordinary skill in the art would not recognize that applicants were in possession of the necessary and common attributes or features of the genus members. Moreover, the claimed genus encompasses metabolites of hormones which are yet to be prepared or envisioned, which further evidences that the disclosed features of the hormone do not constitute support for the claimed genus or a substantial portion of the claimed genus.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claim 72-77, 80-81, 83-88 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claims 72-77, 80-81, 83-88 recite that the hapten and the marker groups or solid phase binding groups are different from each other. This is vague and indefinite as it is unclear what way the groups are to differ from each other. Does applicant intend them to be different by placement, chemical structure or composition etc.? In view of the foregoing, it is not possible to determine the metes and bounds of the claims.

14. Claims 83 and 84 recite the polymeric carriers contain at least one of a positive charge carrier and a negative charge carrier. This is vague and indefinite for two reasons. First, the recitation of the claims sets forth at least one of a series but uses the conjunction 'and' to join the members. As such it is not clear if applicants intend the claim to be read as alt least one of a positive charged or negative charged carrier or at least one of both a positive and negative charge carrier. Second, the claim appears to recite a carrier in the carrier and it is unclear what structure is being set forth here. If applicants mean a charged group they should amend the claim to more clearly recite the structure. In view of the foregoing, it is not possible to determine the metes an bounds of the invention as claimed.

15. Claim 85 recites an essentially helical structure. This is vague and indefinite as it is unclear if applicants intend this to be a structure comprised of a polymeric carrier which consists essentially of an oligomer in helical form or if the carrier is comprised of a polymeric carrier having an essential helical structure. In other words: Does the carrier in its entirety have to be in a

helical form or will a carrier with only a portion in helical form meet the limitations of the claim? In view of the foregoing, it is not possible to determine the metes and bounds of the invention as claimed.

16. Claim 87 recites a hormone metabolite. This vague and indefinite as it is unclear what products will arise upon the metabolism of all hormones in all systems under all conditions of metabolism. As such it is not possible to determine the metes and bound of the invention as claimed.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 72, 74-77, 80-81, 83 and 86 are rejected under 35 U.S.C. 102(b) as being anticipated by Bredehorst et al [Analytical Biochemistry 193(2) 272-278].

Bredehorst et al teach insulin (a polymeric carrier having 2 amino acids) conjugated to a dinitrophenol (DNP) group and three fluorescein molecules coupled to reactive side groups (carboxyl or amine) all at predetermined positions. Therefore, Bredehorst et al anticipate the invention of claims 72, 74-77, 80-81. As the carrier has negatively charged sulfate groups it

anticipates claim 83. As the molecular weight of DNP is in the range of 100-2000 Daltons claim 86 is anticipated.

Note that the statement "wherein the polymeric carrier is prepared by synthesis on a solid phase" does not limit the product as it is directed to a process of making rather than the product and the product can be made by other routes than solid phase synthesis.

19. Applicants' arguments filed 5/30/200 have been fully considered but they are not persuasive.

Applicants assert that because the claims recite the polymeric carrier is synthetically-made Bredehorst et al does not read on the instant claims. This argument has been considered but is not found persuasive as the argument is directed to the process of preparation not the product made. As the product of Bredehorst et al reads on all of the limitations of the rejected claims it anticipates the product set forth in those claims. Therefore, the rejection is maintained for the reasons above and for the reasons of record.

Claim Rejections - 35 USC § 103

20. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

21. Claims 72-77, 80-81, 83-84 and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bredehorst et al in view of Bard et al.[US 5,310,687].

See the teaching of Bredehorst et al *supra.*

Bredehorst et al do not teach the use of luminescent metal chelates as required in an alternative embodiment in claim 81, or as a specific limitation of claims 73 and 84.

However, Bard et al teach the use of luminescent metal chelates as a marker with superior properties for use in assays (See the summary of the invention starting in column 5).

It would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made use the luminescent metal chelates of Bard et al et al in the conjugates as taught Bredehorst et al because Bredehorst et al teach the incorporation of detectable marker groups into conjugates for immuno assays and Bard et al teach the incorporation of luminescent metal chelates into molecules for detecting analyte in immuno assays formats. One of ordinary skill in the art would have been motivated to incorporate the luminescent metal chelates of Bard et al in conjugates as taught by Bredehorst et al in order to take advantage of the rapid efficient and sensitive detection permitted by the chemiluminescent markers taught by Bard et al (see abstract). One of ordinary skill in the art would reasonably have expected to be successful because Bard et al had previously incorporated and applied the chemiluminescence metal chelates to a variety of assays including immunoassay.

22. Claims 72, 74-77, 80-81, 83 and 85-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buchardt *et al* WO 92/20703 in view of Bredehorst *et al* (Analytical Biochemistry 193:272-279).

Buchardt *et al* teach the synthesis and use of peptide nucleic acids or PNA (which reads on nucleotide analogs and amino acids as each monomeric unit of a PNA is an amino acid) wherein the PNA is at made of at least 2 monomers (page 5 line 2), and in a preferred embodiment the length is from 2-61 (page 7 line 10). Buchardt *et al* teach that PNA molecules may be conjugated to reporter ligands including: alkylators, fluorescent compounds, spin labels or protein recognition ligands such as biotin or haptens, which read on marker groups, haptens or solid phase binding groups coupled to reactive side chains (page 20 starting at line 26). Moreover, Buchardt *et al* teach that the L groups (see figure III page 3 for example), which read on groups coupled to reactive side chains, can be a fluorophore, radio or spin label or protein-recognizing ligand such as biotin or a hapten (page 19 lines 5-8). In that each L group is specifically located on the molecule in a location which is determined by the synthetic process under the control of the researcher these groups must be at predetermined positions.

With respect to the dependent claims Buchardt *et al* teach that the oligomers of their invention can be from 2-61 monomers (see page 7, structure III and line 10) which reads on the limitations of claims 74 and 75. In that L groups are explicitly recited as being haptens or fluorophores and as many as 61 L groups are present in a recited preferred embodiment, Buchardt *et al* meet the limitations of claims 76-77. As the terminal groups of the PNA molecules can be acids or amines the reference reads on the limitation of claim 83. Buchardt *et al* teach that the molecule of their invention may be used in a method of capturing a nucleic in a hybridization assay (page 9 line 14 to page 10 line 36), thus the conjugate must be capable of forming a double strand helix and reads on the limitation of claim 85. Buchardt *et al* teach that the molecules of their

invention can be conjugated to a peptide s where the peptides have signaling activity which renders obvious the peptide hormones or peptide epitopes as required by the invention of claim 88.

Buchardt *et al*, while teaching that multiple groups may be incorporated into or conjugated to a PNA molecule, does not explicitly recite incorporating both marker groups and haptens or solid phase binding groups into a single polymeric conjugate molecule.

However, Bredehorst *et al* teach the formation of carrier molecules (conjugates) formed from amino acids with both hapten and multiple marker molecules placed at specific positions see figure 1. Bredehorst et al also specifically recite the incorporation of negatively charge groups (i.e., SO3-, see figure 1) and the use of amino acid based conjugates and Buchardt et al teach the attachment of positive charged (polylysine) and negative charged (carboxyl or sulfo groups) to the carrier molecule; page 20 lines 17-25 which also read further on the limitations of claim 83.

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the invention was made to incorporate both hapten and marker molecules as taught by Bredehorst *et al* in a PNA which is a peptide (and a nucleic acid analog) as taught by Buchardt *et al* because Buchardt *et al* teach the incorporation of haptens and markers into PNA molecules at selected sites and Bredehorst *et al* teach that is it known in the art to incorporate both a hapten and a marker into the same conjugate. One of ordinary skill in the art would have been motivated to do so in order to provide for a sensitive immuno assay of haptens which can quench the fluorophore markers without loss of sensitivity as taught by Bredehorst *et al*. One of ordinary skill in the art would have reasonably expected to be successful because the successful synthesis of PNA

molecules incorporating multiple functionalities at specific positions and the incorporation haptens or markers had previously been taught by Buchardt *et al* and the required placement of a hapten at a position distant enough to prevent quenching of the marker fluorophore would be readily achieved with a PNA molecule.

23. Applicants' arguments filed 8/31/1999 have been fully considered but they are not persuasive. Applicants' have argued that the claims now delete reference to PNA molecules and hence the rejections over Buchardt are moot. This argument is not found persuasive as PNA molecules are comprised of amino acids and hence the reference is still applicable to the instant claims.

24. Claims 72-77, 80-81, and 83-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buchardt et al in view of Bredehorst and further in view of Bard et al.[US 5,310,687].

See the teaching of Buchardt et al in view of Bredehorst et al supra.

Buchardt et al in view of Bredehorst et al do not teach the use of luminescent metal chelates as required in an alternative embodiment in claim 81, or as a specific limitation of claims 73 and 84.

However, Bard et al teach the use of luminescent metal chelates as a marker with superior properties for use in assays (See the summary of the invention starting in column 5).

It would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made use the luminescent metal chelates of Bard et al et al in the conjugates as taught by Buchardt et al in view of Bredehorst et al because Buchardt et al in view of Bredehorst et al teach the incorporation of marker groups into conjugates for immuno assays and Bard et al

teach the incorporation of luminescent metal chelates into molecules for detecting analyte in immuno assays formats. One of ordinary skill in the art would have been motivated to incorporate the luminescent metal chelates of Bard et al in conjugates as taught by Buchardt et al in view of Bredehorst et al in order to take advantage of the rapid efficient and sensitive detection permitted by the chemiluminescent markers taught by Bard et al (see abstract). One of ordinary skill in the art would reasonably have expected to be successful because Bard et al had previously incorporated and applied the chemiluminescence metal chelates to a variety of assays including immunoassay.

Conclusion

25. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Zaun et al US 5,415, 839 teach nucleotides having a hapten and a fluorophore attached.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph W. Ricigliano Ph. D. whose telephone number is (703) 308-9346. The examiner can be reached on Monday through Thursday from 7:00 A.M. to 5:30 P.M.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703) 308-0196.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, can be reached at (703) 308-2439.

Joseph W. Ricigliano Ph. D.

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